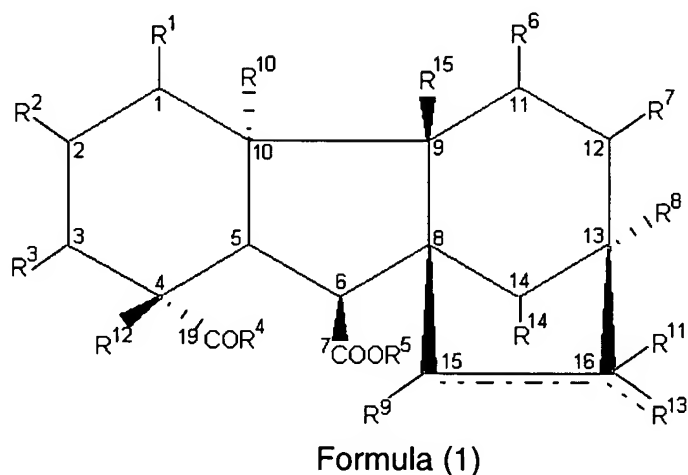


## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application:

### **CLAIMS:**

1. (Currently amended) A method of treatment for diabetes and its complications and associated conditions, including ~~administering~~ administering compounds of Formula (1) (Gibberellins)



wherein

R<sup>1</sup> is H or a group -O-R<sup>20</sup>, where R<sup>20</sup> is H, a glycosyic ether group (glycoside ether), C<sub>1-6</sub> alkyl group, or R<sup>1</sup> together with R<sup>2</sup> or R<sup>10</sup> forms a bond (C<sub>1</sub>-C<sub>2</sub> or C<sub>1</sub>-C<sub>10</sub> double bond, respectively);

R<sup>2</sup> is H or a group -O-R<sup>21</sup>, where R<sup>21</sup> is H, a glycosyic ether group (glycoside ether), or together with R<sup>4</sup> forms a bond (lactone) or R<sup>2</sup> together with R<sup>1</sup> or R<sup>3</sup> forms a bond (C<sub>1</sub>-C<sub>2</sub> or C<sub>2</sub>-C<sub>3</sub> double bond, respectively);

$R^3$  is H, =O, or  $-O-R^{22}$ , where  $R^{22}$  is H or a glycosylic ether group (glycoside ether), or  $R^3$  together with  $R^2$  forms a bond ( $C_2-C_3$  double bond);

$R^4$  is OH, or  $-OR^{23}$ , where  $R^{23}$  is unsubstituted or substituted  $C_{1-20}$  alkyl, allyl, aryl, arylalkyl, amidine,  $-NR^{24}R^{25}$  or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur;  $R^{24}$  and  $R^{25}$  may or may not be the same, are hydrogen, or  $C_{1-20}$  alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or  $R^4$  together with  $R^{21}$  or  $R^{28}$  forms a bond (lactone);

$R^5$  is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted  $C_{1-20}$  alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

$R^6$  is H or OH or together with  $R^7$  forms a bond ( $C_{11}-C_{12}$  double bond);

$R^7$  is H, =O, or  $-OR^{26}$ , where  $R^{26}$  is H or a glycosylic ether group (glycoside ether) or  $R^7$  together with  $R^6$  forms a bond ( $C_{11}-C_{12}$  double bond);

$R^8$  is H, hydroxyl, mercaptan, or halogen, amino, azido,  $NR^{24}R^{25}$ , unsubstituted or substituted  $C_{1-20}$  alkyl, allyl, aryl, or arylalkyl, or  $-OR^{27}$ , where  $R^{27}$  is a glycosylic ether group (glycoside ether);

$R^9$  is H or OH, or together with  $R^{15}$  forms a bond ( $C_9-C_{15}$  bond);

$R^{10}$  is H,  $CH_3$ , CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH,  $CH_2O-R^{28}$  or  $-OR^{28}$ , where  $R^{28}$  is H or together with  $R^4$  forms a bond (lactone) or  $R^{10}$  together with  $R^1$  forms a bond ( $C_1-C_{10}$  double bond);

$R^{11}$  is H, or OH or is absent;

$R^{12}$  is  $CH_3$ ,  $CH_2OH$ ,  $COOH$  or a glycosylic ester (glycoside ester) of said  $COOH$ ;

$R^{13}$  is methylene, or a divalent hetero-atom, or  $NR^{29}$ , where  $R^{29}$  is  $NHR^{30}$  or  $OR^{30}$  where  $R^{30}$  is H, or  $C_{1-20}$  alkyl, aryl, alkylaryl; and a double bond is present between  $C_{16}$  and  $R^{13}$  when  $R^{11}$  is absent; or  $R^{13}$  is H, OH,  $CH_3$  CHO,  $CH_2X$ , where X is halogen,  $CHNR^{29}$  where  $R^{29}$  is  $NHR^{30}$  or  $OR^{30}$  where  $R^{30}$  is H, or  $C_{1-20}$  alkyl, aryl, alkylaryl when  $R^{11}$  is H or OH; with the proviso that where  $R^{11}$  is OH,  $R^{13}$  is not OH;

$R^{14}$  is H or OH;

$R^{15}$  is H, or together with  $R^9$  forms a bond ( $C_9$ - $C_{15}$  bond);

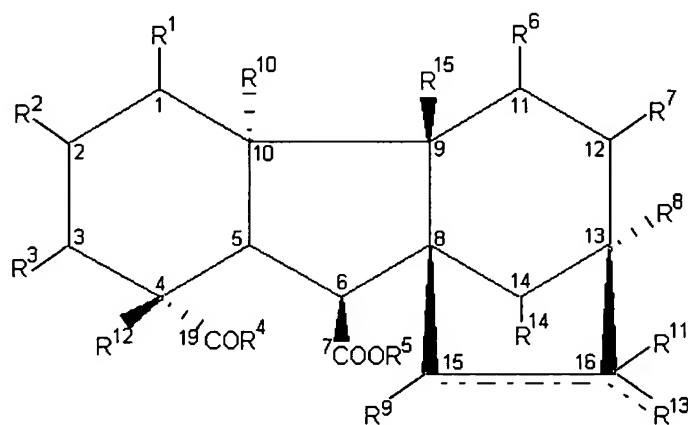
and/or pharmaceutically acceptable derivatives, including lactones, glycosides, esters, active esters and salts thereof, to a patient in need thereof.

2. (Original) The method of claim 1 wherein the complications and associated conditions of diabetes are one or more of: obesity, micro and macro vascular diseases, nephropathy, neuropathy, eye diseases, and diabetic ulcerations.
3. (Original) The method of claim 1, wherein the Gibberellins are Gibberellin  $A_3$ .
4. (Original) The method of claim 1, wherein the Gibberellins are a mixture of Gibberellin  $A_3$  and Gibberellin  $A_4$  and/or Gibberellin  $A_7$ .
5. (Original) The method of claim 1, wherein the pharmaceutically acceptable derivatives are salts including alkali metal salts, alkaline earth metal salts, metal, and salts of ammonium, or organic bases.

6. (Original) The method of claim 5, wherein the organic bases are lidocaine, or  $\text{NR}^{16} \text{R}^{17} \text{R}^{18} \text{R}^{19}$ , where  $\text{R}^{16}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ ,  $\text{R}^{19}$ , which may be the same or not the same, are hydrogen, or substituted or unsubstituted  $\text{C}_{1-20}$  alkyl, alkanol, or aryl groups.

7. (Original) The method of claim 1, wherein the pharmaceutically acceptable derivatives are lactones, glycosides, or esters and active esters.

8. (Currently amended) A method of treatment of diabetes and related conditions including administering an effective amount of a compound of formula (1) (Gibberellins)



Formula (1)

wherein

$\text{R}^1$  is H or a group  $-\text{O}-\text{R}^{20}$ , where  $\text{R}^{20}$  is H, a glycosylic ether group (glycoside ether),  $\text{C}_{1-6}$  alkyl group, or  $\text{R}^1$  together with  $\text{R}^2$  or  $\text{R}^{10}$  forms a bond ( $\text{C}_1-\text{C}_2$  or  $\text{C}_1-\text{C}_{10}$  double bond, respectively);

$\text{R}^2$  is H or a group  $-\text{O}-\text{R}^{21}$ , where  $\text{R}^{21}$  is H, a glycosylic ether group (glycoside ether), or together with  $\text{R}^4$  forms a bond (lactone) or  $\text{R}^2$  together with  $\text{R}^1$  or  $\text{R}^3$  forms a bond ( $\text{C}_1-\text{C}_2$  or  $\text{C}_2-\text{C}_3$  double bond, respectively);

R<sup>3</sup> is H, =O, or -O-R<sup>22</sup>, where R<sup>22</sup> is H or a glycosylic ether group (glycoside ether), or R<sup>3</sup> together with R<sup>2</sup> forms a bond (C<sub>2</sub>-C<sub>3</sub> double bond);

R<sup>4</sup> is OH, or -OR<sup>23</sup>, where R<sup>23</sup> is unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl, amidine, -NR<sup>24</sup>R<sup>25</sup> or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur; R<sup>24</sup> and R<sup>25</sup> may or may not be the same, are hydrogen, or C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or R<sup>4</sup> together with R<sup>21</sup> or R<sup>28</sup> forms a bond (lactone);

R<sup>5</sup> is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted C<sub>1-20</sub> alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

R<sup>6</sup> is H or OH or together with R<sup>7</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>7</sup> is H, =O, or -OR<sup>26</sup>, where R<sup>26</sup> is H or a glycosylic ether group (glycoside ether) or R<sup>7</sup> together with R<sup>6</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>8</sup> is H, hydroxyl, mercaptan, or halogen, amino, azido, NR<sup>24</sup>R<sup>25</sup>, unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, or arylalkyl, or -OR<sup>27</sup>, where R<sup>27</sup> is a glycosylic ether group (glycoside ether);

R<sup>9</sup> is H or OH, or together with R<sup>15</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

R<sup>10</sup> is H, CH<sub>3</sub>, CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH, CH<sub>2</sub>O-R<sup>28</sup> or -OR<sup>28</sup>, where R<sup>28</sup> is H or together with R<sup>4</sup> forms a bond (lactone) or R<sup>10</sup> together with R<sup>1</sup> forms a bond (C<sub>1</sub>-C<sub>10</sub> double bond);

R<sup>11</sup> is H, or OH or is absent;

R<sup>12</sup> is CH<sub>3</sub>, CH<sub>2</sub>OH, COOH or a glycosylic ester (glycoside ester) of said COOH;

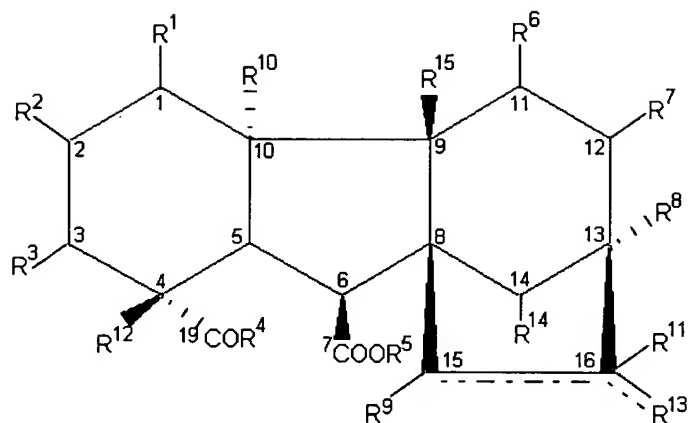
R<sup>13</sup> is methylene, or a divalent hetero-atom, or NR<sup>29</sup>, where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl; and a double bond is present between C<sub>16</sub> and R<sup>13</sup> when R<sup>11</sup> is absent; or R<sup>13</sup> is H, OH, CH<sub>3</sub> CHO, CH<sub>2</sub>X, where X is halogen, CHNR<sup>29</sup> where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl when R<sup>11</sup> is H or OH; with the proviso that where R<sup>11</sup> is OH, R<sup>13</sup> is not OH;

R<sup>14</sup> is H or OH;

R<sup>15</sup> is H, or together with R<sup>9</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

and its pharmaceutically acceptable derivatives to a patient in need thereof.

9. (Original) A method according to claim 8, wherein the Gibberellins are Gibberellin A<sub>3</sub>.
10. (Original) A method according to claim 8, wherein the Gibberellins are a mixture of Gibberellin A<sub>3</sub> and Gibberellin A<sub>4</sub> and/or Gibberellin A<sub>7</sub>.
11. (Currently amended) A method of treatment of diabetes and related conditions comprising administering compounds of formula (1) (Gibberellins)



Formula (1)

wherein

R<sup>1</sup> is H or a group –O-R<sup>20</sup>, where R<sup>20</sup> is H, a glycosylic ether group (glycoside ether), C<sub>1-6</sub> alkyl group, or R<sup>1</sup> together with R<sup>2</sup> or R<sup>10</sup> forms a bond (C<sub>1</sub>– C<sub>2</sub> or C<sub>1</sub>–C<sub>10</sub> double bond, respectively);

R<sup>2</sup> is H or a group –O-R<sup>21</sup>, where R<sup>21</sup> is H, a glycosylic ether group (glycoside ether), or together with R<sup>4</sup> forms a bond (lactone) or R<sup>2</sup> together with R<sup>1</sup> or R<sup>3</sup> forms a bond (C<sub>1</sub>–C<sub>2</sub> or C<sub>2</sub>–C<sub>3</sub> double bond, respectively);

R<sup>3</sup> is H, =O, or –O-R<sup>22</sup>, where R<sup>22</sup> is H or a glycosylic ether group (glycoside ether), or R<sup>3</sup> together with R<sup>2</sup> forms a bond (C<sub>2</sub>–C<sub>3</sub> double bond);

R<sup>4</sup> is OH, or –OR<sup>23</sup>, where R<sup>23</sup> is unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl, amidine, -NR<sup>24</sup>R<sup>25</sup> or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur; R<sup>24</sup> and R<sup>25</sup> may or may not be the same, are hydrogen, or C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or R<sup>4</sup> together with R<sup>21</sup> or R<sup>28</sup> forms a bond (lactone);

R<sup>5</sup> is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted C<sub>1-20</sub> alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

R<sup>6</sup> is H or OH or together with R<sup>7</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>7</sup> is H, =O, or -OR<sup>26</sup>, where R<sup>26</sup> is H or a glycosylic ether group (glycoside ether) or R<sup>7</sup> together with R<sup>6</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>8</sup> is H, hydroxyl, mercaptan, or halogen, amino, azido, NR<sup>24</sup>R<sup>25</sup>, unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, or arylalkyl, or -OR<sup>27</sup>, where R<sup>27</sup> is a glycosylic ether group (glycoside ether);

R<sup>9</sup> is H or OH, or together with R<sup>15</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

R<sup>10</sup> is H, CH<sub>3</sub>, CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH, CH<sub>2</sub>O-R<sup>28</sup> or -OR<sup>28</sup>, where R<sup>28</sup> is H or together with R<sup>4</sup> forms a bond (lactone) or R<sup>10</sup> together with R<sup>1</sup> forms a bond (C<sub>1</sub>-C<sub>10</sub> double bond);

R<sup>11</sup> is H, or OH or is absent;

R<sup>12</sup> is CH<sub>3</sub>, CH<sub>2</sub>OH, COOH or a glycosylic ester (glycoside ester) of said COOH;

R<sup>13</sup> is methylene, or a divalent hetero-atom, or NR<sup>29</sup>, where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl; and a double bond is present between C<sub>16</sub> and R<sup>13</sup> when R<sup>11</sup> is absent; or R<sup>13</sup> is H, OH, CH<sub>3</sub>, CHO, CH<sub>2</sub>X, where X is halogen, CHNR<sup>29</sup> where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl when R<sup>11</sup> is H or OH; with the proviso that where R<sup>11</sup> is OH, R<sup>13</sup> is not OH;

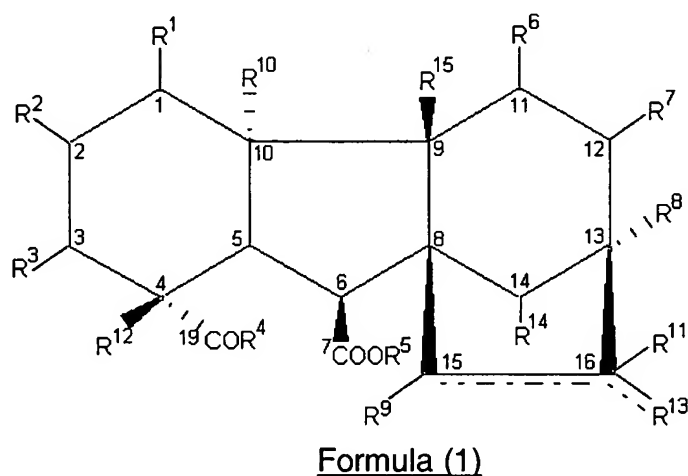
R<sup>14</sup> is H or OH;

R<sup>15</sup> is H, or together with R<sup>9</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);



or their pharmaceutically acceptable derivatives in combination with substances selected from the group consisting of insulin, its fragment derivatives, IGFs, growth factors, and other pharmaceutically compatible anti-diabetic agents, or combinations thereof.

12. (Currently amended) A method of treatment of diabetes and related conditions comprising administering compounds of formula (1) (Gibberellins)



wherein

R<sup>1</sup> is H or a group –O-R<sup>20</sup>, where R<sup>20</sup> is H, a glycosylic ether group (glycoside ether), C<sub>1-6</sub> alkyl group, or R<sup>1</sup> together with R<sup>2</sup> or R<sup>10</sup> forms a bond (C<sub>1</sub>– C<sub>2</sub> or C<sub>1</sub>-C<sub>10</sub> double bond, respectively);

R<sup>2</sup> is H or a group –O-R<sup>21</sup>, where R<sup>21</sup> is H, a glycosylic ether group (glycoside ether), or together with R<sup>4</sup> forms a bond (lactone) or R<sup>2</sup> together with R<sup>1</sup> or R<sup>3</sup> forms a bond (C<sub>1</sub>-C<sub>2</sub> or C<sub>2</sub>-C<sub>3</sub> double bond, respectively);

R<sup>3</sup> is H, =O, or –O-R<sup>22</sup>, where R<sup>22</sup> is H or a glycosylic ether group (glycoside ether), or R<sup>3</sup> together with R<sup>2</sup> forms a bond (C<sub>2</sub>-C<sub>3</sub> double bond);

R<sup>4</sup> is OH, or -OR<sup>23</sup>, where R<sup>23</sup> is unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl, amidine, -NR<sup>24</sup>R<sup>25</sup> or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur; R<sup>24</sup> and R<sup>25</sup> may or may not be the same, are hydrogen, or C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or R<sup>4</sup> together with R<sup>21</sup> or R<sup>28</sup> forms a bond (lactone);

R<sup>5</sup> is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted C<sub>1-20</sub> alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

R<sup>6</sup> is H or OH or together with R<sup>7</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>7</sup> is H, =O, or -OR<sup>26</sup>, where R<sup>26</sup> is H or a glycosylic ether group (glycoside ether) or R<sup>7</sup> together with R<sup>6</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>8</sup> is H, hydroxyl, mercaptan, or halogen, amino, azido, NR<sup>24</sup>R<sup>25</sup>, unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, or arylalkyl, or -OR<sup>27</sup>, where R<sup>27</sup> is a glycosylic ether group (glycoside ether);

R<sup>9</sup> is H or OH, or together with R<sup>15</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

R<sup>10</sup> is H, CH<sub>3</sub>, CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH, CH<sub>2</sub>O-R<sup>28</sup> or -OR<sup>28</sup>, where R<sup>28</sup> is H or together with R<sup>4</sup> forms a bond (lactone) or R<sup>10</sup> together with R<sup>1</sup> forms a bond (C<sub>1</sub>-C<sub>10</sub> double bond);

R<sup>11</sup> is H, or OH or is absent;

R<sup>12</sup> is CH<sub>3</sub>, CH<sub>2</sub>OH, COOH or a glycosylic ester (glycoside ester) of said COOH;

R<sup>13</sup> is methylene, or a divalent hetero-atom, or NR<sup>29</sup>, where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl; and a double bond is present between C<sub>16</sub> and R<sup>13</sup> when R<sup>11</sup> is absent; or R<sup>13</sup> is H, OH, CH<sub>3</sub>, CHO, CH<sub>2</sub>X, where X is halogen, CHNR<sup>29</sup> where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl when R<sup>11</sup> is H or OH; with the proviso that where R<sup>11</sup> is OH, R<sup>13</sup> is not OH;

R<sup>14</sup> is H or OH;

R<sup>15</sup> is H, or together with R<sup>9</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

or their pharmaceutically acceptable derivatives in combination with other compatible therapeutic agents selected from the group consisting of analgesics, anti-hypertensive agents, sedatives, hypnotics, lipid-lowering agents, and anti-infective agents or combinations thereof.

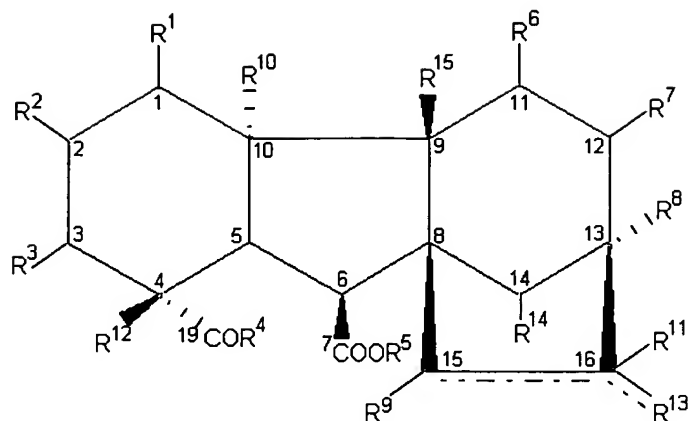
13. (Original) The method according to claim 1, for the treatment of type 1 diabetes and its related conditions.

14. (Original) The method according to claim 1, for the treatment of type 2 diabetes and its related conditions.

15. (Original) The method according to claim 1, for the treatment of insulin resistant diabetes.

16. (Original) The method according to claim 1, for the treatment of diabetic related complications and associated conditions, including obesity, micro and macro vascular diseases, nephropathy, neuropathy and eye diseases.

17. (Currently amended) An anti-diabetic agent comprising a compound of formula (1)



Formula (1)

wherein

R<sup>1</sup> is H or a group –O-R<sup>20</sup>, where R<sup>20</sup> is H, a glycosylic ether group (glycoside ether), C<sub>1-6</sub> alkyl group, or R<sup>1</sup> together with R<sup>2</sup> or R<sup>10</sup> forms a bond (C<sub>1</sub>–C<sub>2</sub> or C<sub>1</sub>–C<sub>10</sub> double bond, respectively);

R<sup>2</sup> is H or a group –O-R<sup>21</sup>, where R<sup>21</sup> is H, a glycosylic ether group (glycoside ether), or together with R<sup>4</sup> forms a bond (lactone) or R<sup>2</sup> together with R<sup>1</sup> or R<sup>3</sup> forms a bond (C<sub>1</sub>–C<sub>2</sub> or C<sub>2</sub>–C<sub>3</sub> double bond, respectively);

R<sup>3</sup> is H, =O, or –O-R<sup>22</sup>, where R<sup>22</sup> is H or a glycosylic ether group (glycoside ether), or R<sup>3</sup> together with R<sup>2</sup> forms a bond (C<sub>2</sub>–C<sub>3</sub> double bond);

R<sup>4</sup> is OH, or –OR<sup>23</sup>, where R<sup>23</sup> is unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl, amidine, –NR<sup>24</sup>R<sup>25</sup> or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur; R<sup>24</sup> and R<sup>25</sup> may or may not be the same, are hydrogen, or C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or R<sup>4</sup> together with R<sup>21</sup> or R<sup>28</sup> forms a bond (lactone);

R<sup>5</sup> is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted C<sub>1-20</sub> alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

R<sup>6</sup> is H or OH or together with R<sup>7</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>7</sup> is H, =O, or -OR<sup>26</sup>, where R<sup>26</sup> is H or a glycosylic ether group (glycoside ether) or R<sup>7</sup> together with R<sup>6</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>8</sup> is H, hydroxyl, mercaptan, or halogen, amino, azido, NR<sup>24</sup>R<sup>25</sup>, unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, or arylalkyl, or -OR<sup>27</sup>, where R<sup>27</sup> is a glycosylic ether group (glycoside ether);

R<sup>9</sup> is H or OH, or together with R<sup>15</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

R<sup>10</sup> is H, CH<sub>3</sub>, CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH, CH<sub>2</sub>O-R<sup>28</sup> or -OR<sup>28</sup>, where R<sup>28</sup> is H or together with R<sup>4</sup> forms a bond (lactone) or R<sup>10</sup> together with R<sup>1</sup> forms a bond (C<sub>1</sub>-C<sub>10</sub> double bond);

R<sup>11</sup> is H, or OH or is absent;

R<sup>12</sup> is CH<sub>3</sub>, CH<sub>2</sub>OH, COOH or a glycosylic ester (glycoside ester) of said COOH;

R<sup>13</sup> is methylene, or a divalent hetero-atom, or NR<sup>29</sup>, where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl; and a double bond is present between C<sub>16</sub> and R<sup>13</sup> when R<sup>11</sup> is absent; or R<sup>13</sup> is H, OH, CH<sub>3</sub>, CHO, CH<sub>2</sub>X, where X is halogen, CHNR<sup>29</sup> where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl when R<sup>11</sup> is H or OH; with the proviso that where R<sup>11</sup> is OH, R<sup>13</sup> is not OH;

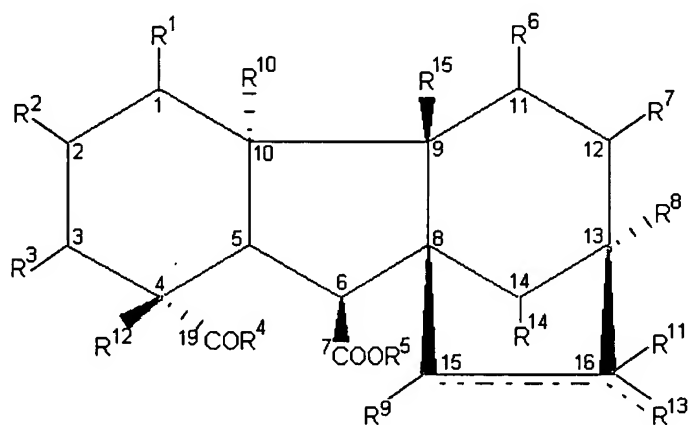
R<sup>14</sup> is H or OH;

R<sup>15</sup> is H, or together with R<sup>9</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

and/or its derivatives as an active ingredient, together with a pharmaceutically acceptable carrier.

18. (Original) An anti-diabetic agent according to claim 17, wherein the agent is a medicament suitable for administration with a medicator.

19. (Currently amended) An anti-diabetic agent comprising a compound of formula (1)



Formula (1)

wherein

R<sup>1</sup> is H or a group -O-R<sup>20</sup>, where R<sup>20</sup> is H, a glycosylic ether group (glycoside ether), C<sub>1-6</sub> alkyl group, or R<sup>1</sup> together with R<sup>2</sup> or R<sup>10</sup> forms a bond (C<sub>1</sub>-C<sub>2</sub> or C<sub>1</sub>-C<sub>10</sub> double bond, respectively);

R<sup>2</sup> is H or a group -O-R<sup>21</sup>, where R<sup>21</sup> is H, a glycosylic ether group (glycoside ether), or together with R<sup>4</sup> forms a bond (lactone) or R<sup>2</sup> together with R<sup>1</sup> or R<sup>3</sup> forms a bond (C<sub>1</sub>-C<sub>2</sub> or C<sub>2</sub>-C<sub>3</sub> double bond, respectively);

R<sup>3</sup> is H, =O, or –O-R<sup>22</sup>, where R<sup>22</sup> is H or a glycosylic ether group (glycoside ether), or R<sup>3</sup> together with R<sup>2</sup> forms a bond (C<sub>2</sub>-C<sub>3</sub> double bond);

R<sup>4</sup> is OH, or –OR<sup>23</sup>, where R<sup>23</sup> is unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl, amidine, -NR<sup>24</sup>R<sup>25</sup> or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur; R<sup>24</sup> and R<sup>25</sup> may or may not be the same, are hydrogen, or C<sub>1-20</sub> alkyl, allyl, aryl, arylalkyl or an unsaturated or saturated ring containing one or more hetero-atoms selected from the group consisting of nitrogen, oxygen and sulphur; or R<sup>4</sup> together with R<sup>21</sup> or R<sup>28</sup> forms a bond (lactone);

R<sup>5</sup> is H or a glycosylic ester (glycoside ester) group, or unsubstituted or substituted C<sub>1-20</sub> alkyl esters, allyl esters, aryl esters, arylalkyl esters, active esters;

R<sup>6</sup> is H or OH or together with R<sup>7</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>7</sup> is H, =O, or –OR<sup>26</sup>, where R<sup>26</sup> is H or a glycosylic ether group (glycoside ether) or R<sup>7</sup> together with R<sup>6</sup> forms a bond (C<sub>11</sub>-C<sub>12</sub> double bond);

R<sup>8</sup> is H, hydroxyl, mercaptan, or halogen, amino, azido, NR<sup>24</sup>R<sup>25</sup>, unsubstituted or substituted C<sub>1-20</sub> alkyl, allyl, aryl, or arylalkyl, or –OR<sup>27</sup>, where R<sup>27</sup> is a glycosylic ether group (glycoside ether);

R<sup>9</sup> is H or OH, or together with R<sup>15</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

R<sup>10</sup> is H, CH<sub>3</sub>, CHO, COOH, or a glycosylic ester (glycoside ester) of said COOH, CH<sub>2</sub>O-R<sup>28</sup> or –OR<sup>28</sup>, where R<sup>28</sup> is H or together with R<sup>4</sup> forms a bond (lactone) or R<sup>10</sup> together with R<sup>1</sup> forms a bond (C<sub>1</sub>-C<sub>10</sub> double bond);

R<sup>11</sup> is H, or OH or is absent;

R<sup>12</sup> is CH<sub>3</sub>, CH<sub>2</sub>OH, COOH or a glycosylic ester (glycoside ester) of said COOH;

R<sup>13</sup> is methylene, or a divalent hetero-atom, or NR<sup>29</sup>, where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl; and a double bond is present between C<sub>16</sub> and R<sup>13</sup> when R<sup>11</sup> is absent; or R<sup>13</sup> is H, OH, CH<sub>3</sub>, CHO, CH<sub>2</sub>X, where X is halogen, CHNR<sup>29</sup> where R<sup>29</sup> is NHR<sup>30</sup> or OR<sup>30</sup> where R<sup>30</sup> is H, or C<sub>1-20</sub> alkyl, aryl, alkylaryl when R<sup>11</sup> is H or OH; with the proviso that where R<sup>11</sup> is OH, R<sup>13</sup> is not OH;

R<sup>14</sup> is H or OH;

R<sup>15</sup> is H, or together with R<sup>9</sup> forms a bond (C<sub>9</sub>-C<sub>15</sub> bond);

as an active ingredient, together with pharmaceutically acceptable carriers or excipients, wherein the agent is a slow release composition.

20. (Original) An anti-diabetic agent according to claim 17, wherein the agent is for oral administration.

21. (Original) An anti-diabetic agent according to claim 17, wherein the agent is for inhalation administration.

22. (Original) An anti-diabetic agent according to claim 17, wherein the agent is for transdermal administration.

23. (Original) An anti-diabetic agent according to claim 17, wherein the agent is for parenteral injection.

24. (Original) An anti-diabetic agent according to claim 17, wherein the agent is for topical, rectal, or vaginal administration.



25. (Original) An anti-diabetic agent according to claim 17, wherein the derivative of formula (1) is selected from the group consisting of lactones, esters, alkali metal salts, alkaline earth metal salts, transition metal salts, ammonium salts and organic bases.
26. (Original) An anti-diabetic agent according to claim 25 wherein the derivative is a sodium salt of formula (1).
27. (Original) An anti-diabetic agent according to claim 25 wherein the derivative is a zinc salt of formula (1).
28. (Original) An anti-diabetic agent according to claim 25 wherein the derivative is a ethyl ester of formula (1).
29. (Original) A method of manufacturing an anti-diabetic agent according to claim 17, comprising combining a compound of formula (1) and/or its derivatives with a pharmaceutically acceptable carrier.
30. (Original) A process for the preparation of Gibberellins including Gibberellin A<sub>3</sub>, including the steps of:
- (a) incubating a Gibberellin-producing strain of microorganism in a fermentation broth;
  - (b) adjusting the pH of the fermentation broth to pH 6.5 to 7.0 and filtering to obtain a filter cake of microorganism mycelium, and a filtrate;
  - (c) washing the filter cake with water and combining the washing with the filtrate to form an aqueous solution;
  - (d) concentrating the aqueous solution;
  - (e) mixing the aqueous solution with an organic solvent at a temperature of 5 to 10°C and adjusting the pH of the mixture to less than 2.0;
  - (f) allowing the mixture to separate into an aqueous phase and a first organic phase and removing the first organic phase;

- (g) re-extracting the aqueous phase from step (f) with organic solvent to obtain a second organic phase;
  - (h) combining the first and second organic phases and concentrating to form a concentrated organic solution;
  - (i) heating the concentrated organic solution at 60-70°C for 3 to 4 hours with stirring, until the precipitation of solid matter ceases;
  - (j) cooling the concentrated organic solution to room temperature and filtering to obtain a precipitate;
  - (k) washing the precipitate in cold organic solvent and drying to obtain an off-white solid containing about 80% Gibberellin A<sub>3</sub>, about 4% Gibberellin A<sub>4</sub> and about 4% Gibberellin A<sub>7</sub>.
31. (Original) The process of claim 30, comprising the further steps of:
- (l) dissolving the off-white solid in a mixture of 32.6% methanol, 2.2% water and 65.2% acetone to obtain a Gibberellin solution;
  - (m) diluting the Gibberellin solution with a 10:1 mixture of organic solvent and water;
  - (n) filtering the diluted Gibberellin solution and concentrating the filtrate by vacuum evaporation;
  - (o) heating the concentrate to a temperature of 60 to 80°C for 2 to 3 hours with stirring, cooling to room temperature and filtering to obtain a solid crystalline precipitate;
  - (p) washing the precipitate with cold organic solvent and drying to obtain Gibberellin A<sub>3</sub> crystals.
32. (Original) A process according to claim 30 wherein the Gibberellin-producing strain of microorganism is *Gibberella fujikuroi*.
33. (Original) A process according to claim 30, wherein the concentration of the solutions in steps (d) and (h) is achieved using vacuum evaporation.

34. (Original) A process according to claim 30 wherein the organic solvent is ethyl acetate.
35. (Original) A process according to claim 31 wherein the organic solvent is ethyl acetate.
36. (Original) A process according to claim 31 comprising the further steps of:
- (q) dissolving the Gibberellin A<sub>3</sub> in methanol;
  - (r) adding the Gibberellin solution to an equimolar aqueous solution of NaHCO<sub>3</sub>;
  - (s) evaporating the mixed solutions to dryness to obtain a solid residue;
  - (t) dissolving the residue in water and freeze drying to obtain Gibberellin A<sub>3</sub> sodium salt.
37. (Original) A process according to claim 36, comprising the further steps of dissolving the Gibberellin A<sub>3</sub> sodium salt in water, passing the solution through a column loaded with a zinc ion-exchange resin, washing the column with water, collecting and combining the effluent and washings and removing the water to obtain Gibberellin A<sub>3</sub> zinc salt.
38. (Original) A process according to claim 31 comprising the further steps of:
- (q) dissolving the Gibberellin A<sub>3</sub> in a 50:1 ratio mixture of acetone to water;
  - (r) mixing the Gibberellin A<sub>3</sub> solution with equimolar amounts of triethylamine and ethyl chloroformate, and a one tenth molar amount of N-methyl morpholine, and stirring at -15°C for 20 minutes;
  - (s) diluting the resultant mixture with anhydrous ethanol and stirring at room temperature;
  - (t) evaporating the diluted mixture to dryness and partitioning the residue between ethyl acetate and water in a 6:1 ratio;

separating the ethyl acetate layer, washing with 2% HCl, followed by water, followed by 5% NaHCO<sub>3</sub>, followed by water, and evaporating under reduced pressure to dryness to give Gibberellin A<sub>3</sub> ethyl ester.